

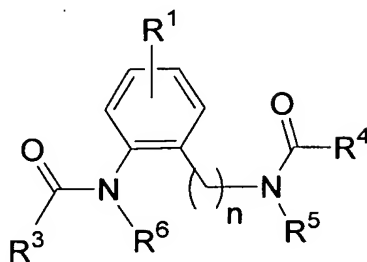
AMENDMENTS TO THE CLAIMS

Please amend the claims as follows.

Listing of Claims:

Claims 1-51. (Canceled)

52. (New) A compound of the formula I:



wherein:

R¹ is selected from the group consisting of:

- (1) hydrogen,
- (2) halogen,
- (3) C₁-6alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (4) -OC₁-6alkyl,
- (5) -S(O)_m-C₁-6alkyl, wherein m is selected from 0, 1 and 2,
- (6) -CO₂R⁹, wherein R⁹ is independently selected from:
 - (a) hydrogen,
 - (b) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
 - (c) benzyl, and
 - (d) phenyl,
- (7) -NR¹⁰R¹¹, wherein R¹⁰ and R¹¹ are independently selected from:
 - (a) hydrogen,
 - (b) -C₁-6alkyl, which is unsubstituted or substituted with 1-6 fluoro,
 - (c) -C₅-6cycloalkyl,
 - (d) benzyl,
 - (e) phenyl,
 - (f) -S(O)₂-C₁-6alkyl,
 - (g) -S(O)₂-benzyl, and
 - (h) -S(O)₂-phenyl,

- (8) $-S(O)_2-NR^{10}R^{11}$,
- (9) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) $-C_{1-6}$ alkyl,
 - (b) $-O-C_{1-6}$ alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl, and
 - (f) $-OCF_3$;

R^3 is selected from the group consisting of:

- (1) C_{1-6} alkyl, which is substituted with halogen, hydroxyl or phenyl,
- (2) C_{3-7} cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and
- (3) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) $-C_{1-6}$ alkyl, which is unsubstituted or substituted with $-NR^{10}R^{11}$,
 - (b) $-O-C_{1-6}$ alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) $-OCF_3$;
 - (g) $-CO_2R^9$,
 - (h) $-NR^{10}R^{11}$,
 - (i) $-C(O)NR^{10}R^{11}$, and
 - (j) $-NO_2$,
- (4) heterocycle, wherein heterocycle is selected from:
benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxalinyl, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholinyl, thiomorpholinyl,

dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinolinyl, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:

- (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- (d) hydroxy,
- (e) phenyl,
- (f) trifluoromethyl,
- (g) -OCF₃;
- (h) -CO₂R⁹,
- (i) -NR¹⁰R¹¹, and
- (j) -CONR¹⁰R¹¹;

R⁴ is selected from the group consisting of:

- (1) C₁₋₆alkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl,
- (2) C₃₋₇cycloalkyl, which is unsubstituted or substituted with halogen, hydroxyl or phenyl, and
- (3) phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:
 - (a) -C₁₋₆alkyl,
 - (b) -O-C₁₋₆alkyl,
 - (c) halo,
 - (d) hydroxy,
 - (e) trifluoromethyl,
 - (f) -OCF₃,
 - (g) -CO₂R⁹,
 - (h) -NR¹⁰R¹¹,
 - (i) -CONR¹⁰R¹¹, and
 - (j) -NO₂;
- (4) heterocycle, wherein heterocycle is selected from:

benzoimidazolyl, benzimidazolonyl, benzofuranyl, benzofurazanyl, benzopyrazolyl, benzotriazolyl, benzothiophenyl, benzoxazolyl, carbazolyl, carbolinyl, cinnolinyl, furanyl, imidazolyl, indolinyl, indolyl, indolaziny, indazolyl, isobenzofuranyl, isoindolyl, isoquinolyl, isothiazolyl, isoxazolyl, naphthpyridinyl, oxadiazolyl, oxazolyl, oxazoline, isoxazoline, oxetanyl, pyranyl, pyrazinyl, pyrazolyl, pyridazinyl, pyridopyridinyl, pyridazinyl, pyridyl, pyrimidyl, pyrrolyl, quinazolinyl, quinolyl, quinoxaliny, tetrahydropyranyl, tetrazolyl, tetrazolopyridyl, thiadiazolyl, thiazolyl, thienyl, triazolyl, azetidiny, 1,4-dioxanyl, hexahydroazepinyl, piperazinyl, piperidinyl, pyridin-2-onyl, pyrrolidinyl, morpholinyl, thiomorpholinyl, dihydrobenzoimidazolyl, dihydrobenzofuranyl, dihydrobenzothiophenyl, dihydrobenzoxazolyl, dihydrofuranyl, dihydroimidazolyl, dihydroindolyl, dihydroisooxazolyl, dihydroisothiazolyl, dihydrooxadiazolyl, dihydrooxazolyl, dihydropyrazinyl, dihydropyrazolyl, dihydropyridinyl, dihydropyrimidinyl, dihydropyrrolyl, dihydroquinoliny, dihydrotetrazolyl, dihydrothiadiazolyl, dihydrothiazolyl, dihydrothienyl, dihydrotriazolyl, dihydroazetidiny, methylenedioxybenzoyl, tetrahydrofuranyl, and tetrahydrothienyl, and N-oxides thereof, which is unsubstituted or substituted with one or more substituents independently selected from:

- (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- (d) hydroxy,
- (e) phenyl,
- (f) trifluoromethyl,
- (g) -OCF₃,
- (h) -CO₂R⁹,
- (i) -NR¹⁰R¹¹, and
- (j) -CONR¹⁰R¹¹;

or wherein R⁴ and R⁵ are joined together to form a phthalimidyl, succinimidyl or glutamidyl ring, which is unsubstituted or substituted with one or more substituents independently selected from the definitions of R²;

R² is selected from the group consisting of:

- (1) hydrogen,
- (2) -C₁₋₆alkyl,
- (3) -O-C₁₋₆alkyl,
- (4) halo,

- (5) hydroxyl,
- (6) -NO₂, and
- (7) phenyl;

R⁵ and R⁶ are independently selected from the group consisting of:

- (1) hydrogen, and
- (2) C₁-6alkyl;

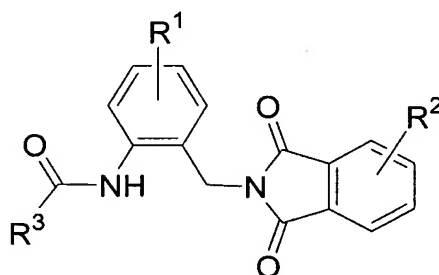
n is an integer selected from 1, 2 and 3;

with the proviso that the compound of formula I is not:

N-[4-chloro-2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl]-acetamide,
N-[2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]-4-methylphenyl]-acetamide, or
N-[2-[(1,3-dihydro-1,3-dioxo-2H-isoindol-2-yl)methyl]phenyl]-acetamide;

or a pharmaceutically acceptable salt thereof.

53. (New) The compound of Claim 52 of the formula Ia:



Ia

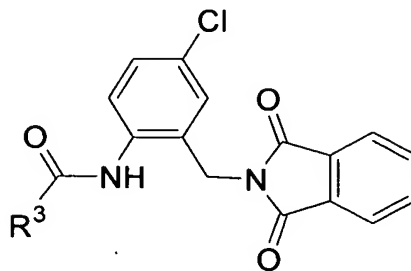
wherein

R² is selected from the group consisting of:

- (1) hydrogen,
- (2) -C₁-6alkyl,
- (3) -O-C₁-6alkyl,
- (4) halo,
- (5) hydroxyl,
- (6) -NO₂, and
- (7) phenyl;

or a pharmaceutically acceptable salt thereof.

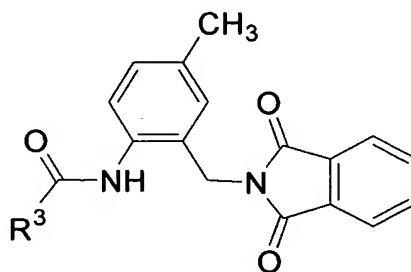
54. (New) The compound of Claim 52 of the formula Ib:



Ib

or a pharmaceutically acceptable salt thereof.

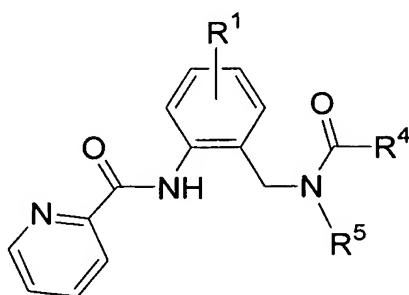
55. (New) The compound of Claim 52 of the formula Ic:



Ic

or a pharmaceutically acceptable salt thereof.

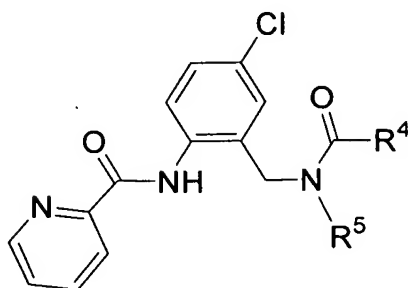
56. (New) The compound of Claim 52 of the formula Id:



Id

or a pharmaceutically acceptable salt thereof.

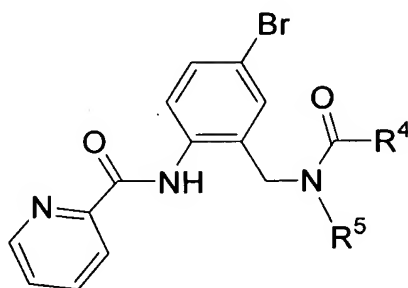
57. (New) The compound of Claim 52 of the formula Ie:



Ie

or a pharmaceutically acceptable salt thereof.

58. (New) The compound of Claim 52 of the formula If:



If

or a pharmaceutically acceptable salt thereof.

59. (New) The compound of Claim 52 wherein R¹ is hydrogen.

60. (New) The compound of Claim 52 wherein R² is halo.

61. (New) The compound of Claim 60 wherein R² is fluoro.

62. (New) The compound of Claim 60 wherein R² is chloro.

63. (New) The compound of Claim 60 wherein R² is bromo.

64. (New) The compound of Claim 52 wherein R² is methyl.

65. (New) The compound of Claim 52 wherein R³ is phenyl, which is unsubstituted or substituted with one or more substituents independently selected from:

- (a) -C₁₋₆alkyl,
- (b) -O-C₁₋₆alkyl,
- (c) halo,
- (d) hydroxy,
- (e) trifluoromethyl,
- (f) -OCF₃;
- (g) -CO₂-C₁₋₆alkyl,
- (h) -NH₂,
- (i) -NH-C₁₋₆alkyl,
- (j) -CONH₂, and
- (k) -CONH-C₁₋₆alkyl.

66. (New) The compound of Claim 65 wherein R³ is phenyl, which is unsubstituted or substituted with hydroxy, halo, -CONHC₁₋₆alkyl or -CO₂C₁₋₆alkyl.

67. (New) The compound of Claim 52 wherein R³ is pyridyl, pyrimidinyl, pyrazinyl, pyridazinyl, piperazinyl, furanyl or thienyl.

68. (New) The compound of Claim 52 wherein R⁴ and R⁵ are joined together to form a phthalimidyl ring.

69. (New) The compound of Claim 52 wherein R⁵ is hydrogen or C₁₋₆alkyl.

70. (New) The compound of Claim 52 wherein R⁶ is hydrogen.

71. (New) The compound of Claim 52 wherein n is 1.

72. (New) A compound which is selected from the group consisting of:
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-hydroxybenzamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyrimidine-2-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-hydroxybenzamide;

2-[(2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl)amino]carbonyl]phenyl;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-2-hydroxybenzamide;
2-chloro-N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}benzamide;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-2-fluorobenzamide;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}benzamide;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-3-fluorophenyl}-3,5-difluorobenzamide;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-3-methoxybenzamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-methylbenzamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-2-furamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-5-methylisoxazole-3-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}cyclohexanecarboxamide;
N-{5-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}cyclohexanecarboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1-methyl-1H-imidazole-2-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1,3-thiazole-4-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-3-hydroxypyridine-2-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}imidazo[2,1-b][1,3]thiazole-6-carboxamide;
N-{4-chloro-2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}-1,2,5-thiadiazole-3-carboxamide;
N-{2-[(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-methoxyphenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(4-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(2,5-dioxo-3-phenyl-2,5-dihydro-1H-pyrrol-1-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(4-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(5,6-dimethyl-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(5-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-chloro-2-[(5-ethoxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;

N-{5-bromo-3-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]pyridin-2-yl}pyridine-2-carboxamide;
N-{4-chloro-2-[(5-hydroxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(5-fluoro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(5-ethoxy-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(4,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{2-[(4,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-fluorophenyl}pyridine-2-carboxamide;
N-{2-[(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]-4-fluorophenyl}pyridine-2-carboxamide;
N-{4-fluoro-2-[(5-nitro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{4-bromo-2-[(4-methyl-1,3-dioxo-3,4,5,6-tetrahydrocyclopenta[c]-pyrrol-2(1H)-yl)methyl]phenyl}pyridine-2-carboxamide;
N-{5-bromo-2-[(pyridin-2-ylcarbonyl)amino]benzyl}pyridine-2-carboxamide;
N-(4-bromo-2-[(2-fluorobenzoyl)amino]methyl}phenylpyridine-2-carboxamide;
N-{5-bromo-2-[(pyridin-2-ylcarbonyl)amino]benzyl}pyridine-2-carboxamide;
N-[4-bromo-2-({[2-(trifluoromethyl)benzoyl]amino}methyl)phenyl]-pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,5-dichlorobenzoyl)(ethyl)amino]methyl}phenyl})-pyridine-2-carboxamide;
N-(2-{{[(4-butoxybenzoyl)(ethyl)amino]methyl}-4-chlorophenyl})-pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,5-dimethoxybenzoyl)(ethyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,4-dichlorobenzoyl)(ethyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,5-dichlorobenzoyl)(isobutyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,5-dimethoxybenzoyl)(isobutyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-{5-fluoro-2-[(pyridin-2-ylcarbonyl)amino]benzyl}quinoxaline-2-carboxamide;
N-(2-{{[(4-butoxybenzoyl)amino]methyl}-4-fluorophenyl})pyridine-2-carboxamide;
N-(4-bromo-2-{{[(3-methoxybenzoyl)(methyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-(4-chloro-2-{{[(3,5-dichlorobenzoyl)(methyl)amino]methyl}phenyl})pyridine-2-carboxamide;
N-(2-{{[[3,5-bis(trifluoromethyl)benzoyl](methyl)amino]methyl}-4-chlorophenyl})pyridine-2-carboxamide;
N-[4-chloro-2-({[(3,5-dichlorobenzoyl)[2-(dimethylamino)ethyl]amino}methyl)-phenyl]pyridine-2-carboxamide;
N-[2-(benzoylamino)-5-bromobenzyl]-N,3,5-trimethylbenzamide;

N-(4-bromo-2-[[[(3,5-dichlorobenzoyl)(methyl)amino]methyl]-phenyl]pyridine-2-carboxamide;

N-(4-bromo-2-[[[(3,4-difluorobenzoyl)(methyl)amino]methyl]phenyl]-pyridine-2-carboxamide;

N-(4-bromo-2-[[[(2,4-difluorobenzoyl)(methyl)amino]methyl]phenyl]-pyridine-2-carboxamide;

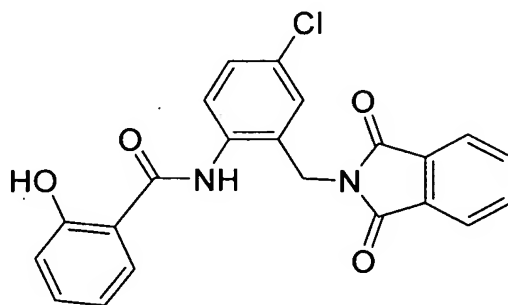
N-(4-bromo-2-[[[(3,4-dichlorobenzoyl)(methyl)amino]methyl]phenyl]-pyridine-2-carboxamide;

N-[4-chloro-2-({methyl[2-(trifluoromethyl)benzoyl]amino}methyl)-phenyl]pyridine-2-carboxamide;

N-(4-chloro-2-[[[(3,4-dichlorobenzoyl)(methyl)amino]methyl]-phenyl]pyridine-2-carboxamide;

or a pharmaceutically acceptable salt thereof.

73. (New) A compound which is:



or a pharmaceutically acceptable salt thereof.

74. (New) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 52 or a pharmaceutically acceptable salt thereof.

75. (New) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 72 or a pharmaceutically acceptable salt thereof.

76. (New) A method for potentiation or inhibition of metabotropic glutamate receptor activity in a mammal which comprises the administration of an effective amount of the compound of Claim 52 or a pharmaceutically acceptable salt thereof.

77. (New) A method for treating, controlling, or reducing the risk of schizophrenia in a mammalian patient in need of such which comprises administering to the patient a therapeutically effective amount of a compound of Claim 52 or a pharmaceutically acceptable salt thereof.